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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,399	07/01/2003	John R. Desjarlais	A-71273-3/RMS/RMK 463077-	1891
32940	7590	04/18/2006	EXAMINER	
DORSEY & WHITNEY LLP 555 CALIFORNIA STREET, SUITE 1000 SUITE 1000 SAN FRANCISCO, CA 94104			EMCH, GREGORY S	
			ART UNIT	PAPER NUMBER
			1649	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,399	DESJARLAIS ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-26,33 and 36-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-26,33 and 36-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 July 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/02/04</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignment A</u> . |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 17-26, 33, and 36-44 in the reply filed on 02 February 2006 is acknowledged. Applicant's elections without traverse of the species: I. BLyS, II. Position 66 in the large domain, position 97 in the small domain, position 87 in the DE loop, and position 57 in the trimer interface and III. A large domain and DE loop without the trimer interface in the reply filed on 02 February 2006 are also acknowledged.

Formal Matters

Claims 1-16, 27-32, 34 and 35 were canceled in the reply filed on 02 February 2006. Currently, claims 17-26, 33, and 36-44 are pending and under consideration.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

This application is claiming the benefit of prior-filed nonprovisional application no. 10/338,083 under 35 U.S.C. 120, 121, or 365(c).

MPEP Chapter 201.11 states: "There are six conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, 121, or 365(c) or under 35 U.S.C.

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119(e)...(B) With respect to claiming benefit under 35 U.S.C. 120, 121, or 365(c), the later-filed application must be copending with the prior application or with an application similarly entitled to the benefit of the filing date of the prior application."

In the instant case, Applicant claims priority as a continuation in part to U.S. Patent Application No. 10/338,083, filed on 01/06/2003, which claims benefit of 60/345,805, which was filed on 01/04/2002 and thus expired on 01/04/2003. Thus, no co-pendency was established with the earlier provisional application to which benefit was claimed. Therefore, the benefit of the earlier filing date (01/04/2002) is denied.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 02 November 2004 is enclosed in this action.

Specification

The disclosure is objected to because of the following informalities:

The disclosure, including but not limited to pages 5, 6, 7 14-16 and 19, refers to sequences that are set forth in Applicant's sequence listing. MPEP 37 CFR 1.821 (d) states, "Where the description or claims of a patent application discuss a sequence that is set forth in the 'Sequence Listing' in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by 'SEQ ID NO:' in the text of the description or claims."

Appropriate correction is required.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-20, 23-26, 33, and 36-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 50-58 and 64-72 of copending Application No. 09/981,289. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '289 Application claims variant TNF- α proteins with amino acid

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substitutions that are of the same scope as the variant TNFSF proteins of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 18, 23-26, 33, and 36-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/963,994. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '994 Application claims compositions comprising variant human TNF- α proteins with amino acid substitutions that are of the same scope as the variant TNFSF proteins of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17, 18, 24, 33, and 36-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/008,091. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '091 Application claims a variant human TNF- α protein comprising the amino acid substitution F144N (in the trimer interface and large domain) and is hence of the same scope as the variant TNFSF proteins of the instant claims.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-26, 33, and 36-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to variant TNFSF monomer proteins and mixed TNFSF oligomers comprising at least one variant TNFSF protein and a naturally occurring TNFSF protein.

According to the specification, the proteins of the instant invention are members of the Tumor Necrosis Factor Super Family (TNFSF) with antagonist activity (p.1, lines 11-39). Further, the present invention provides variant TNFSF proteins comprising an amino acid sequence that has at least one modification as compared to the naturally

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occurring TNFSF protein sequence, wherein said variant proteins will physically interact with naturally occurring TNFSF proteins to form mixed oligomers substantially incapable of activating receptor signaling (p.2, lines 36-39). The TNFSF currently constitutes at least 18 cytokines that exist in membrane bound and secreted forms, i.e., proteins that are cleaved from the membrane to release the extracellular domain as a regulator (p.1, lines 11-39). Also, at p.7, lines 21-39, extracellular domain is defined as the segment of protein existing predominantly outside the cell, generally soluble when cleaved or isolated away from the rest of the protein. Alternatively, the extracellular domain could comprise the whole protein or amino acid segments thereof when secreted from the cell and can be defined functionally, as a TNFSF protein or variant that is soluble and will form oligomers, preferably with wild-type monomers. Further, at p. 11, lines 19-30, modifications are made to the TNFSF proteins, such that the ability of the variant protein to interact with and sequester the naturally occurring TNFSF protein is preserved. Preferably, these modifications will enhance the ability of the variant TNFSF proteins to hetero-oligomerize with one or more naturally occurring TNFSF proteins.

The specification and claims do not set forth the structure of the multitude of TNFSF variants and oligomers that are encompassed by the invention; thus, these are genus claims. The scope of the claims includes numerous structural variants, and the genera are highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claims do not provide guidance as to what changes should be made. Structural features that could

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distinguish compounds in the claimed genera from others in the amino acid class are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of each genus, and because each genus is highly variant, a variant TNFSF protein and a mixed TNFSF oligomer are insufficient to describe the genera. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genera. Thus, Applicants were not in possession of the claimed genera.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "a variant TNFSF protein according to claims 18-26". It is unclear whether this limitation is intended to encompass the limitations of any of one of claims 18 through 26, or all of the limitations of claims 18 through 26, or the limitations of 18 and 26, etc. The metes and bounds of the claim thus cannot be ascertained. The claim should refer to claims 18-26 in the alternate.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17-26, 33, and 36-44 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to variant TNFSF monomer proteins and mixed TNFSF oligomers comprising at least one variant TNFSF protein and a naturally occurring TNFSF protein.

The claims as written encompass molecules that may already be present in nature. Applicants are not in possession of any and all variants and oligomers of TNFSF proteins. It is noted that incorporating the term "isolated" may obviate the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-25, 33 and 36-44 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,171,787 to Wiley.

The claims are drawn to variant TNFSF monomer proteins and mixed TNFSF oligomers comprising at least one variant TNFSF protein and a naturally occurring TNFSF protein.

The '787 patent discloses a TNFSF protein that is 28.7% homologous with Applicant's SEQ ID NO: 8, with non-conservative mismatches at, for example, positions 29, 34, 84, 91, and 97, thus meeting the limitations of claims of 18, 24, 36, and 38-43 (see sequence alignment A). The '787 patent teaches that approximately the first 150 N-terminal amino acids are located in the receptor contact position (col.1, lines 52-61). Thus, since the mismatches recited *supra* occur within these residues as well as within the trimer interface domain, and since modifications in the receptor contact region and the trimer interface domain would encompass surface modifications, claims 23, 37 and 38 are anticipated. Furthermore, the '787 patent discloses pharmaceutical compositions for administration in a subject, thus meeting the limitation of claim 33 (col. 8, lines 30-37; col.30, lines 6-19).

The '787 patent also discloses naturally purified TNFSF proteins (col.40, lines 17-28), variants of said proteins (col.40, lines 29-46), and oligomers, trimers, dimers and higher order oligomers of said naturally purified TNFSF proteins and variants (col.40, lines 47-52), thus meeting the limitations of claims 17, 22, and 25. Furthermore, the '787 patent discloses synthetic fragments with or without substitutions, which inhibit activation of the TNFSF polypeptide or the TNFSF receptor and discloses that said

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polypeptide can be a soluble fragment, which is capable of binding a receptor for TNF-gamma (col.4, lines 31-39; col.31, line 66 – col.32, line 21). Thus, since inhibitors that bind to soluble TNFSF polypeptides that normally bind to a TNFSF receptor are contemplated, the limitations of claims 19-21 and 44 have been met.

Since the patent discloses all the elements of the claims, claims 17-25, 33 and 36-44 are anticipated by U.S. Patent No. 6,171,787 to Wiley.

Claims 17, 18, 19, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,716,805 to Srinivasan et al.

The claims are drawn to variant TNFSF monomer proteins and mixed TNFSF oligomers comprising at least one variant TNFSF protein and a naturally occurring TNFSF protein.

The '805 patent discloses fusion proteins comprising the extracellular portion of members of the TNFSF (col.2, lines 56-67) and that the extracellular domain is modified by fusing a leucine zipper sequence to said domain (col.7, lines 50-52), thus meeting the limitations of claim 18. The '805 patent also discloses homo-oligomers and hetero-oligomers of cytokines (col.3, lines 1-52), thus meeting the limitations of claims 17, 25 and 26. Further, the '805 patent discloses soluble forms of the proteins that are useful as receptor antagonists by binding to the cognate receptor and preventing signaling (col.3, lines 64-67), thus meeting the limitations of claim 19.

Since the patent discloses all the elements of the claims, claims 17, 18, 19, 25 and 26 are anticipated by U.S. Patent No. 5,716,805 to Srinivasan et al.

Conclusion

No claims are allowed.

References

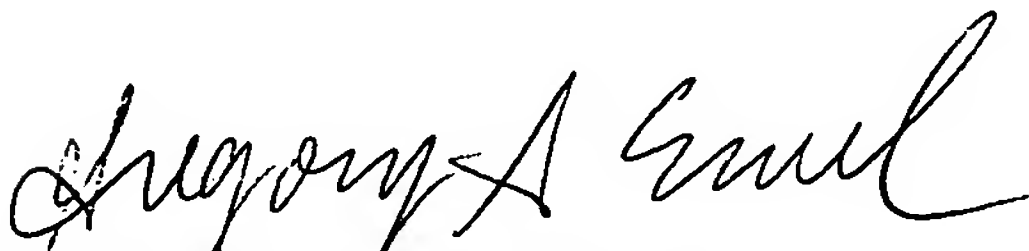
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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
April 11, 2006


JANET L. ANDRES
SUPERVISORY PATENT EXAMINER